

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, and listings, of claims in the application. Please amend Claims 1, 2, 7, 14, and 16. Please add Claims 18-30.

Listing of Claims

1. (Currently amended) A method for identifying cell matrix signaling (CMS) pathway induced genes that are modulated during vascular or proliferative diseases and related disorders comprising:

(a) adding one or more vascular disease stimuli to a first cell culture of endothelial cells;

(b) adding one or more vascular disease stimuli to a second cell culture of smooth muscle cells;

(c) adding one or more vascular disease stimuli to a third cell culture of endothelial cells and smooth muscle cells in co-culture;

(d) measuring the amount of vascular disease markers in (a), (b), and (c); and

(e) comparing the amount of the vascular disease markers in (a), (b), and (c) to each other and to ~~co-cultures~~ controls of untreated ~~cells~~ cell cultures or co-cultures.

2. (Currently amended) The method of Claim 1, wherein the vascular disease stimuli is are AGE, insulin, IL-1 β , or TNF- α or a any combination thereof.

3. (Original) The method of Claim 1, wherein the vascular disease marker is interleukin 6 (IL-6), interferon-inducible protein-10 (IP-10), monokine induced by gamma-interferon (MIG), interferon-inducible T-cell alpha chemoattractant (I-TAC), vascular adhesion molecule-1 (VCAM-1), or monocyte chemoattractant protein-1 (MCP-1).

4. (Original) The method of Claim 1, wherein the smooth muscle cells are layered over the endothelial cells in co-culture.

5. (Original) The method of Claim 4, wherein the smooth muscle cells and the endothelial cells are layered in a specific ratio.

6. (Original) The method of Claim 5, wherein the ratio is 1:1, 1:2, 1:3, or 1:4.

7. (Currently amended) A method for identifying compounds that regulate CMS pathway induced genes comprising:

(a) adding one or more vascular disease stimuli and a test compound ~~with unknown effects on endothelial cells~~ to a first cell culture of endothelial cells;

(b) adding one or more vascular disease stimuli and a the test compound ~~with unknown effects on smooth muscle cells~~ to a second cell culture of smooth muscle cells;

(c) adding one or more vascular disease stimuli and a the test compound to a third cell culture of endothelial cells and smooth muscle cells in co-culture;

(d) measuring the amount of vascular disease markers in (a), (b), and (c); and

(e) comparing the amount of the vascular disease markers in (a), (b), and (c) to controls of untreated cells and co-cultures each other and to endothelial cells, smooth muscle cells, and co-cultures thereof which are untreated, treated with only test compound, or treated with only vascular and proliferative disease stimuli.

8. (Currently amended) The method of claim 7, wherein the vascular disease stimuli is are AGE, insulin, IL-1 β , or TNF α or a any combination thereof.

9. (Original) The method of claim 7, wherein the vascular disease marker is IL-6, IP-10, MIG, I-TAC, VCAM-1, or MCP-1.

10. (Original) The method of Claim 7, wherein the test compound is an oligonucleotide, ribozyme, antisense oligonucleotide, peptide, peptoid, small organic molecule, or small inorganic molecule.

11. (Original) The method of Claim 10, wherein the test compound is an oligonucleotide complementary to the 5' region of the CMS pathway induced gene.

12. (Original) The method of Claim 10, wherein the test compound is a ribozyme molecule that blocks translation of the CMS pathway induced gene.

13. (Original) The method of Claim 10, wherein the test compound binds the protein product of the CMS induced gene.

14. (Currently amended) A method of diagnosing a vascular or proliferative disease or related disorder comprising:

- (a) measuring the level of transcription of CMS pathway induced genes present in a patient or patient sample and in a corresponding control sample; and
- (b) comparing the level of CMS pathway induced genes transcript in both samples; wherein if the level of transcript detected differs in the patient sample relative to the corresponding control sample, a vascular disease or a related disorder is diagnosed.

15. (Original) A method of diagnosing a vascular or proliferative disease or related disorder comprising:

- (a) measuring CMS pathway induced gene product protein level or protein activity present in a patient or patient sample and in a corresponding control sample; and
- (b) comparing the CMS pathway induced gene product protein level or protein activity in both samples;

wherein if the level of protein or protein activity detected differs in the patient or patient sample relative to the corresponding control sample, a proliferative disease or an oncogenic related disorder is diagnosed.

16. (Currently amended) A method for monitoring the efficacy of treatment for a vascular or proliferative disease or related disorder comprising:

- (a) measuring the amount of vascular disease markers in a patient sample from a patient with a vascular disease, proliferative disease, or related disorder;
- (b) treating a the patient for the vascular or proliferative disease;
- (c) measuring the amount of vascular disease markers in patient samples taken during treatment; and
- (d) comparing the amount of vascular disease markers in (a) to (c).

17. (Original) The method of Claim 16, wherein the vascular disease marker is IL-6, IP-10, MIG, I-TAC, VCAM-1, or MCP-1.

18. (New) A method of treating or preventing inflammation comprising administering an effective amount of a pharmaceutical composition comprising one or more compounds determined by the method of Claim 7.

19. (New) The method of Claim 18, wherein the composition further comprises an auxiliary which is a diluent, binder, stabilizer, buffer, salt, lipophilic solvent, preservative, adjuvant, anti-oxidant, bacteriostat, solute, suspending agent, or thickening agent.

20. (New) The method of Claim 18, wherein the composition is in a form suitable for administration by oral, parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracelebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic,

intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transmermal means.

21. (New) The method of Claim 18, wherein the composition is in the form of a tablet, capsule, microcapsules, solution, suspension, emulsion, lozenge, cream, gel, paste, pastille, foam, spray, pessary, tamport, or suppository.

22. (New) The method of Claim 18, wherein the pharmaceutical composition is administered in combination with other therapeutic agents.

23. (New) A method for regulating protein expression of a CMS pathway induced gene comprising:

(a) identifying one or more compounds which regulate CMS pathway induced genes by the method of Claim 7; and

(b) administering an effective amount of a composition containing one or more of said compounds to a patient.

24. (New) A method for identifying compounds that regulate CMS pathway induced gene protein product activity comprising:

(a) adding one or more vascular or proliferative disease stimuli and a test compound to a first cell culture of endothelial cells;

(b) adding one or more vascular or proliferative disease stimuli and the test compound to a second cell culture of smooth muscle cells;

(c) adding one or more vascular or proliferative disease stimuli and the test compound to a co-culture of endothelial cells and smooth muscle cells;

(d) measuring the amount of CMS pathway induced gene protein product activity in (a), (b), and (c); and

(e) comparing the amount of CMS pathway induced gene protein product activity in (a), (b), and (c) to each other and to endothelial cell cultures, smooth muscle cell cultures and co-cultures of endothelial cells and smooth muscle cells which are untreated, treated with only test compound, or treated with only vascular and proliferative disease stimuli.

25. (New) A method for regulating an activity of a protein product of a CMS pathway induced gene comprising:

(a) identifying one or more compounds which affect the activity of CMS pathway induced gene protein products by the method of Claim 24; and

(b) administering an effective amount of one or more of said compounds to a patient.

26. (New) A method of diagnosing a vascular or proliferative disease or related disorder comprising:

(a) measuring the level of transcription of CMS pathway induced genes present in a patient sample and in a corresponding control sample; and

(b) comparing the level of CMS pathway induced genes transcript in both samples; wherein if the level of transcript detected differs in the patient sample relative to the corresponding control sample, a vascular disease or a related disorder is diagnosed.

27. (New) The method of Claim 7, wherein the test compound has an unknown effect on smooth muscle cells, an unknown effect on endothelial cells, or an unknown effect on both smooth muscle cells and endothelial cells.

28. (New) The method of Claim 1, wherein the one or more vascular disease stimuli is a single vascular disease stimulus.

29. (New) The method of Claim 7, wherein the one or more vascular disease stimuli is a single vascular disease stimulus.

30. (New) The method of Claim 24, wherein the one or more vascular disease stimuli is a single vascular disease stimulus.